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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 11/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/733,692	MURPHY ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *180-222* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *180-222* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 December 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application. This application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid. Applicant's submission filed on August 26, 2005 has been entered. Claims 180-222 are pending and under examination. The cancellation of claims 1-180 renders all previous rejections of claims 1-180 moot.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 190-195 and 213-217 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to chimeric viruses, specifically wherein the substitution mutation at position 456 of the L protein is "to another amino acid". The breadth of the claims has not been adequately described such that one of skill in the art would know how to practice the invention.

The specification describes a mutation wherein the amino acid at position 456 of PIV3 is changed to leucine. However, Applicant's claims encompass a substitution of any of the 20 amino acids. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is one example (456 F) out of 20 possibilities and no particular function. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 180-222 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite, "attenuated for replication at least 10-fold in the respiratory tract of a primate host infected with said chimeric PIV". This limitation is unclear because it lacks comparative basis for the term "10-fold". The metes and bounds of the claims cannot be determined without a standard to which attenuation may be measured.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 180-189, 196-212 and 218-220 are rejected under 35 U.S.C. 102(e) as being anticipated by Belshe *et al.* (US 5,869,036, "Belshe"). The claims are directed to infectious chimeric parainfluenza virus (polynucleotides encoding them, vectors and methods of making) comprising a major nucleocapsid protein (N), a nucleocapsid phosphoprotein (P), a large polymerase protein (L), and a partial or complete PIV3 genome or antigenome combined with

one or more heterologous gene(s) or genome segment(s) encoding a complete open reading frame or one or more antigenic determinant(s) of one of more heterologous pathogen(s) operably linked to regulatory sequences operable in said chimeric PIV genome or antigenome; said infectious chimeric PIV having a wild type L protein and being attenuated for replication at least 10-fold in the respiratory tract of a primate host compared to wild type HPIV3.

Belshe contemplates the use of the hybrid viruses as immunogenic compositions (abstract). Belshe teaches hybrid *cp*45 viruses and methods of producing the viruses comprising an enveloped, negative-sense, single-stranded chimeric RNA genome, which includes N, P and L genes (see Belshe claims). Specific *cp*45 mutations that are contemplated by Belshe are His for Tyr at residue 942, and Phe for Leu at residue 992, represented by Applicant's SEQ ID NO: 69 and 71. Belshe's constructs use the cp45 background genome as a template for recombination. The *cp*45 genome contains all of the mutations instantly claimed (SEQ ID NO: 55, 57, 59, 61, 63, 65, 67, 69, 71 and 73). Heterologous sequences of other PIVs, such as HPIV-1, HPIV-2, RSV, Influenza A and B, Measles virus, and BPIV3 are substituted for their counterparts in the HPIV-3 *cp*45 genome (abstract, col. 8, lines 54-58, and col. 17 and 18). Substitution of a counterpart gene, for example the HN gene, would require that the entire open reading frame be inserted somewhere between the HN and L open reading frames.

Regarding the limitation of 10-fold attenuation of replication, Applicant points to Table 11, page 102, of the specification. Table 11 discloses levels of replication in the upper and lower respiratory tract of hamsters using various constructs of wild type and mutant PIV3 viruses. Applicant's specification teaches that the majority of mutations in the L gene are responsible for the attenuated phenotype of the cp45 virus. Applicant also teaches that other mutations outside

of the L gene also contribute to the cp45 attenuated phenotype. While Belshe does not demonstrate levels of attenuated replication, the hybrid viruses that Belshe describes are expected to have the property of attenuated replication of at least 10-fold. One would reasonably expect Belshe's hybrid constructs to have this characteristic because the structural features of the viruses of Belshe and the structural features of Applicant's constructs are the same as claimed. For example, Belshe's cp45 hybrid virus contains the mutation A450T in the F protein. Applicant's construct having the A450T mutation in the F protein had at least a 10-fold attenuation of replication (instant specification, Table 11).

Belshe's construct is a cp45 genome with a wild type L gene introduced. Viruses were recovered and were attenuated, thus demonstrating that the wild type L gene was not entirely responsible for attenuation (Example 5, Belshe). The cp45 genome necessarily contains mutations in genes other than the L gene, thus reading on the instant claims.

Given the disclosure of Belshe and the breadth of the instant claims, the claims are anticipated by Belshe.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 196-201 and 218-222 rejected under 35 U.S.C. 103(a) as being unpatentable over Belshe. The claims are drawn to embodiments described above, wherein the heterologous gene

segments are inserted operatively linked to a gene start and a gene end sequence of the PIV background genome. This limitation does not lend patentability to the claimed invention because insertion of heterologous gene encoding the antigenic determinant would only be appropriate between a gene start and gene end sequence. One would have been motivated to use the gene start and gene end sequences of Belshe's background PIV in order to retain as much stability as possible when expressing the heterologous genes. One would have had a reasonable expectation of success given the fundamental nature of recombination and the desire to obtain stable expression. Therefore, the claimed subject matter would have been obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

6. Applicant's arguments and observations are primarily directed to the following:

- Applicant discloses that the recovery of Belshe's hybrid *cp*45 viruses was performed by a complementation assay wherein a plasmid expressing wild-type HPIV3 L protein provided a very small degree of recovery of virus plaques.
    - In response to this observation, the examiner agrees that the viruses were recovered. Regardless of the amount recovered, Belshe did recover virus (col. 8, lines 21-25). The claims do not require a particular amount of virus be produced.
- Applicant points out that Belshe's disclosure regarding hybrid *cp*45 viruses is limited to Example 7, and the mention of exchanging heterologous surface glycoproteins for those on the PIV genome.

- In response to this observation, the specification describes a method of making the virus using the *cp*45 virus genome as a background genome into which other genes may be inserted (co. 9-10).

- Applicant points out that Belshe's explanation for attenuation is mutation of the L protein, not the wild-type. Applicant asserts that Belshe does not contemplate any attenuated virus obtained by mutating other than the L protein. In contrast, Applicant's claims are directed to embodiments wherein the L protein is the wild-type, and the virus remains attenuated due to other temperature-sensitive mutations.
  - In response to this observation, Example 5 of the Belshe patent discloses the introduction of the wild type L gene into the *cp*45 genome. Belshe recovered virus that contained a wild type L gene and also contained mutation in gene other than the L gene. Because the *cp*45 genome necessarily contains mutations in other genes besides the L gene, the introduction of the wild type L gene resulted in a virus that expressed the wild type L protein along with the other mutations that are naturally present in the *cp*45 virus (col. 8, lines 21-25).
- Applicant argues that Belshe does not provide the concept of inserting the heterologous gene encoding an open reading frame between the GS and GE sequences of the background PIV.
  - In response to this assertion, it would have been obvious for one of ordinary skill in the art to insert the heterologous sequence between a gene start and gene end sequence. One would have been motivated to use the gene start and gene end sequences of Belshe's background PIV in order to retain as much stability as

possible when expressing the heterologous genes. One would have had a reasonable expectation of success given the fundamental nature of recombination and the desire to obtain stable expression.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 180-222 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 144-215 of copending Application No. 09/083,793. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is encompasses the embodiments set forth in the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 180-222 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 53-85 of copending Application No. 09/458,813. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is encompasses the embodiments set forth in the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. Claims 180-222 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-30 and 46-74 of copending Application No. 09/459,062. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is encompasses the embodiments set forth in the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 180-222 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 84-163 of copending Application No. 09/586,479. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is a species of the instantly claimed genus of PIVs, rendering the genus claims obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

11. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Stacy B. Chen
November 14, 2005